

1 162. A method for producing a recombinant respiratory syncytial virus (RSV)
2 from one or more isolated polynucleotide molecules encoding said RSV, comprising:

3 expressing in a cell or cell-free lysate an expression vector comprising an
4 isolated polynucleotide comprising a recombinant RSV genome or antigenome which is
5 modified by a partial or complete gene deletion, a change in gene position, or one or more
6 nucleotide change(s) that modulate expression of a selected gene.

1 163. The method of claim 162, wherein the recombinant RSV genome or
2 antigenome and the N, P, L and RNA polymerase elongation factor proteins are expressed by
3 two or more different expression vectors.--

REMARKS

Status of the Claims

With entry of this Preliminary Amendment claims 1-62 have been canceled and new claims 63-163 have been added consistent with the restriction requirement mailed on December 10, 1997 in the above identified parent application and to more distinctly set forth the subject matter of the invention toward which this divisional application is directed.

The present claims encompass in part subject matter identified by the Office as representing Group II specified in the restriction requirement in the parent application. This Group was characterized by the Office to embrace recombinant RSV with a modified SH gene and dependent claims related thereto. Applicants' Preliminary Amendment presented herein incorporates this subject matter as well as additional, related subject matter. Based on the characterization of this subject matter presented below, Applicants respectfully submit that all of the claims set forth in this Preliminary Amendment should be examined, without further restriction, in a single application. In particular, the claims presented herein above bear sufficient relationship that it will not be unduly burdensome for the Office to examine all of the claims together on the merits. Coordinate review of the claims now presented will in fact facilitate the Office's review and provide for consistent examination of the subject matter presented.

As a preliminary point in addressing the Restriction Requirement imposed in the parent application, Applicants note that no reference was made by the Office therein to aspects of the invention that are clearly related to the identified Group II (RSV having a deletion of an SH gene). For example, claims 12 and 51 are nowhere listed or discussed among the proposed groupings in the Restriction Requirement. These claims are generically directed to recombinant RSV wherein "a SH, NS1, NS2 or G gene is modified" (claim 12) and to methods "to ablate or modulate expression of a SH, NS1, NS2 or G gene or a cis-acting regulatory sequence." Other claims were originally presented that relate more broadly or narrowly to this subject matter, which are all clearly supported by the specification. Applicants respectfully submit that the instant claims distinctly define this subject matter within a related set of compositions and methods directed to RSV having "a modification . . . introduced within the genome or antigenome comprising a partial or complete gene deletion, a change in gene position, or one or more nucleotide change(s) that modulate expression of a selected gene."

Among these related compositions and methods, Applicants' specification describes RSV having modifications that comprise a partial or complete gene deletion (e.g., deletion of a SH, NS1, NS2, or G gene). Alternatively, gene expression can be modulated (i.e., upregulated or downregulated at the transcriptional or translational level) by "introduction of one or more translation termination codons", "introduction of a frame shift mutation", "introduction, modification or ablation of a translational start site", or by changing a "position of one or more gene(s) in the genome or antigenome". It is these and similarly related aspects of the invention to which the present claims are directed. Within these related aspects, more detailed aspects of the invention are represented in the dependent claims (e.g., RSV possessing changes that modulate gene expression as above, which are further modified . . . to incorporate attenuating mutations, to incorporate a non-RSV gene, or to incorporate a nucleotide deletion, insertion, substitution, rearrangement, or modification of a cis-acting regulatory sequence within the recombinant RSV genome or antigenome).

Thus, the claims presented above are believed to be consistent with the Restriction Requirement in the parent application, at least to the extent that the Restriction Requirement substantively addressed the subject matter of the original claims. The claims now presented for consideration are clearly related in fundamental aspects. Further restriction or species segregation of these claims would impose an undue burden on Applicants and result in

a protracted, uncoordinated review process. In contrast, although certain aspects of the claims may be separate and distinct, no undue burden would be imposed on the Office to prosecute these claims together on their merits in a single application. The respective subject matter of the claims presented herein does not present "a separate subject for inventive effort, and also a separate field of search" (see, e.g., MPEP § 808.02).

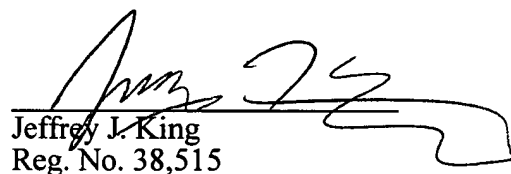
Formal Corrections

In addition to the claims amendments presented herein, typographical amendments have been presented in the specification correcting the amino acid residue change specified by a mutation substituting C for A at nucleotide position 6313. This mutation which encodes a mutation substituting Ala for Glu at amino acid position 218 was incorrectly specified as a substitution of Asp for Glu at position 218 in Tables 37 and 38 of the specification. The amendments above correct an obvious error and are consistent with the correct designation of the noted mutation (i.e., substituting Ala, not Asp, for Glu at position 218) provided elsewhere in the specification, e.g., at Table 39.

The claims presented above are all believed to be in condition for allowance. Early notice to that effect is earnestly solicited. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the subject application, the Examiner is invited to telephone the undersigned at 206/467-9600.

Respectfully submitted,

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Jeffrey J. King
Reg. No. 38,515

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (206) 467-9600
Fax: (415) 576-0300

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